CLAIMS

What is claimed is:

1. A reagent array chip comprising a substrate with a self-assembled monolayer formed at an interface on a surface of the substrate; and an array of reagents in removable contact with the self-assembled monolayer.

2. The array chip of claim **1**, wherein the substrate comprises glass and the interface comprises gold.

3. The array chip of claim **1**, wherein the interface comprises glass and the self-assembled monolayer comprises a silane.

4. The array chip of claim **1**, wherein the interface comprises gold or silver, and the self-assembled monolayer comprises a sulfide, a thiol, or a disulfide.

5. The array chip of claim **1**, wherein the self-assembled monolayer comprises an alkane thiol.

6. The array chip of claim **5**, wherein the self-assembled monolayer comprises 1-undecane thiol, 1-hexadecane thiol, 16 mercapto-1-hexadecanol, or 11-mercapto-1-undecanol.

7. The array chip of claim **1**, wherein the interface comprises a metal oxide and the self-assembled monolayer comprises a fatty acid.

8. The array chip of claim **1**, wherein the interface comprises a phosphate and the self-assembled monolayer comprises a phosphonate.

9. The array chip of claim **1**, wherein at least one reagent is selected from the group consisting of a protein, a nucleic acid, a cytokine, a receptor, a pharmaceutical, a virus, a buffer, a co-factor, a modulator, an inhibitor, an activator, a chemical, and a compound.

10. A reagent library spotted to the array chip of claim **1**.

11. The array chip of claim **1**, further comprising one or more alignment marks.

12. The array chip of claim **11**, wherein the alignment marks are water insoluble.

13. The array chip of claim **11**, wherein the alignment marks comprise a polymer excipient insoluble in aqueous solvents, and a dye present in an amount sufficient to render the mark substantially opaque.

14. The array chip of claim **11**, wherein reagents are spotted onto the self-assembled monolayer in fixed register with respect to the alignment marks.

15. The array chip of claim **14**, wherein the distance between adjacent spotted reagent locations is not more than about 0.9 mm as measured center to center.

16. The array chip of claim **14**, wherein the distance between adjacent spotted reagent locations is not more than about 0.5 mm as measured center to center.

17. The array chip of claim **1**, further comprising a patterned region on the substrate surface wherein the self-assembled monolayer is formed, and an unpatterned region wherein the self-assembled monolayer is excluded from at least a portion of the unpatterned region.

18. The array chip of claim **17**, further comprising a second self-assembled monolayer formed in the unpatterned region and substantially excluded from the patterned region.

19. A method of spotting reagents, the method comprising:

forming a self-assembled monolayer at an interface on a surface of a substrate; and,

spotting reagents onto the self-assembled monolayer.

20. The method of claim **19**, wherein forming a self-assembled monolayer comprises contacting the interface with a solution or depositing a vapor onto the interface.

21. The method of claim **19**, wherein the interface comprises glass and the self-assembled monolayer comprises a silane.

22. The method of claim **19**, wherein the interface comprises gold or silver, and the self-assembled monolayer comprises a sulfide, a thiol, or a disulfide.

23. The method of claim **22**, wherein the self-assembled monolayer comprises an alkane thiol, or a hydroxy-terminal alkane thiol.

24. The method of claim **19**, wherein the interface comprises a metal oxide and the self-assembled monolayer comprises a fatty acid.

25. The method of claim **19**, wherein the interface comprises a phosphate and the self-assembled monolayer comprises a phosphonate.

26. The method of claim **19**, wherein the reagent comprises a protein, a nucleic acid, a cytokine, a receptor, a pharmaceutical, a virus, a buffer, a co-factor, a modulator, an inhibitor, an activator, a chemical, or a compound.

27. The method of claim **19**, further comprising:

adding reaction mixture constituents to the reagents: and,

detecting chemical reactions in the reaction mixture.

28. The method of claim **19**, further comprising:

drying the reagents;

dissolving the dried reagents; and,

collecting the dissolved reagents from the self-assembled monolayer;

thereby recovering the reagents from the self-assembled monolayer.

29. The method of claim **28**, wherein the reagents are not permanently bound to the self-assembled monolayer.

30. The method of claim **28**, wherein the steps of forming a self-assembled monolayer, spotting, drying, dissolving, collecting, or transferring are carried out using an automated instrument.

31. The method of claim **28**, further comprising:

selecting the self-assembled monolayer to provide a desired characteristic in association with a particular reagent composition;

wherein the desired characteristic is selected from the group consisting of: contact angle, consistent spot size, even distribution of the reagents, spot roundness, consistent recovery of a reagent, and efficient recovery of a reagent.

32. The method of claim **31**, wherein selecting the self-assembled monolayer comprises:

preparing a series of two or more self assembling monolayer formulations;

contacting the formulations to one or more test interfaces, thereby forming monolayers at the test interfaces;

applying the reagent composition to the monolayers;

measuring a characteristic outcome; and,

determining which monolayer better provides the desired characteristic outcome;

thereby selecting the self-assembled monolayer.

33. The method of claim **32**, wherein the self assembling monolayer formulations comprise two or more molecules with different hydrophobicity.

34. The method of claim **32**, wherein:

the self assembling monolayer formulations comprise molecules with a substrate binding group, an alkane group, and a terminal group;

the alkane group comprising a carbon chain ranging in length from about 3 carbons to about 22 carbons; and,

the terminal group comprising a hydrophilic or hydrophobic chemical structure.

35. The method of claim **32**, wherein the self assembling monolayer formulations comprise an alkane thiol or a hydroxyl terminal alkane thiol.

36. A reagent library array comprising:

a chip substrate with a surface comprising a patterned interface and an unpatterned interface; and,

at least one self-assembled monolayer formed in the patterned interface or the unpatterned interface; and,

an array of reagents spotted on the self-assembled monolayer.

37. The library array of claim **36**, wherein the one interface comprises glass and the other interface comprises gold.

38. The library array of claim **36**, wherein the patterned interface or the unpatterned interface comprises gold, and the self-assembled monolayer comprises an alkane thiol.

39. The library array of claim **36**, wherein the patterned interface or the unpatterned interface comprises glass, and the self-assembled monolayer comprises a silane.

40. A reagent library spotted to the library array of claim **36**.

41. A method of preparing a reagent library on a chip, the method comprising:

forming a patterned interface on a surface of a chip substrate;

forming a self-assembled monolayer on the patterned interface or an unpatterned interface of the substrate surface; and,

spotting one or more reagents to the self-assembled monolayer on the patterned interface or on the self-assembled monolayer on the unpatterned interface;

thereby providing a reagent library.

42. The method of claim **41**, wherein forming a patterned interface comprises photolithography.

43. The method of claim **41**, wherein forming a patterned interface comprises etching.

44. The method of claim **43**, wherein the etching comprises application of etchant solution to the chip.

45. The method of claim **41**, wherein forming a patterned interface comprises sputtering, depositing, or electroplating a pattern onto a chip surface through a patterned film, mask or a stencil.

46. The method of claim **41**, wherein the chip substrate comprises a chromium adhesion layer.

47. The method of claim **46**, further comprising applying a layer of gold to the chip substrate, by sputtering or thermal evaporation, prior to forming the patterned interface.

48. The method of claim **41**, wherein the interface on the surface of a chip substrate comprises a metal selected from the group consisting of gold, silver, copper, and germanium.

49. The method of claim **41**, wherein the patterned interface or unpatterned interface comprises glass, plastic, silicon or a polymer.

50. The method of claim **41**, wherein forming a self-assembled monolayer comprises contacting one or more chip interfaces with a self assembling monolayer formulation optimized to provide high or consistent recovery of the reagents from the library.

51. The method of claim **50**, wherein the self assembling monolayer formulation comprises a solution or a vapor.

52. The method of claim **41**, wherein the patterned interface comprises reagent spotting locations.

53. The method of claim **52**, wherein the patterned interface is more hydrophobic than the unpatterned interface.

54. The method of claim **52**, wherein the patterned interface is less hydrophobic than the unpatterned interface.

55. The method of claim **41**, wherein the unpatterned interface comprises reagent spotting locations.

56. The method of claim **55**, wherein the patterned interface is more hydrophobic than the unpatterned interface.

57. The method of claim **55**, wherein the patterned interface is less hydrophobic than the unpatterned interface.

58. The method of claim **41**, wherein the molecules which form a self-assembled monolayer are selected from a group consisting of alkane thiols, and Silanes.

59. The method of claim **58**, wherein the alkane thiol comprises a hydroxyl group.

60. The method of claim **41**, wherein the distance between adjacent reagents spotted to the self assembling monolayers is not more than about 0.9 mm as measured center to center.

61. The method of claim **41**, wherein the distance between adjacent reagents spotted to the self assembling monolayers is not more than about 0.5 mm as measured center to center.

62. The method of claim **41**, wherein the reagents are selected from a group consisting of a protein, a nucleic acid, a pharmaceutical, a virus, a buffer, a co-factor, a modulator, an inhibitor, an activator, a chemical, and a compound.

63. The method of claim **41**, further comprising:

drying the reagents;

dissolving the reagents by contacting the dry reagents with a solvent; and,

collecting the dissolved reagents;

thereby recovering the reagents from the library.

64. The method of claim **63**, wherein the steps of forming a pattern, forming a self-assembled monolayer, spotting, drying, dissolving, collecting, or transferring are carried out using an automated instrument.

65. A composition for application of alignment marks to a substrate, the composition comprising:

a non aqueous solvent;

a dye soluble in the solvent; and,

a polymer excipient soluble in the solvent;

wherein the composition forms a water insoluble mark when dried on the substrate.

66. The composition of claim **65**, wherein the solvent is selected from the group consisting of DMSO, DMF, an alcohol, and acetonitrile.

67. The composition of claim **65**, wherein the dye is selected from the group consisting of acridine, analine, anthraquinone, arylmethane, azo, diazonium, graphite, indulin, imine, nitro, phthalocyanine, quinone, tetrazolium, thiazole, and xanthene.

68. The composition of claim **67**, wherein the dye is present in an amount ranging from about 1 weight percent to about 20 weight percent of the total composition.

69. The composition of claim **68**, wherein the dye is present in an amount ranging from about 3 weight percent to about 15 weight percent of the total composition.

70. The composition of claim **69**, wherein the dye is present at about 10 weight percent of the total composition.

71. The composition of claim **65**, wherein the polymer selected from the group consisting of polyvinyl, glucan, glycan, polyester, polysaccharide, polycycloalkylene, polyether, and polyanhydride.

72. The composition of claim **71**, wherein the polymer is present in an amount ranging from about 0.5 weight percent to about 10 weight percent of the total composition.

73. The composition of claim **72**, wherein the polymer is present in an amount ranging from about 1 weight percent to about 5 weight percent of the total composition.

74. The composition of claim **73**, wherein the polymer is present at about 2 weight percent of the total composition.

75. An alignment marked substrate comprising:

a substrate with a surface; and,

one or more alignment marks comprising a substantially water insoluble polymer excipient, and a dye present in an amount sufficient to render the alignment mark substantially opaque, on the surface of the substrate.

76. The marked substrate of claim **75**, further comprising an array of one or more reagents, wherein the array is arranged on the substrate surface at locations in a fixed register with respect to the alignment marks.

77. The marked substrate of claim **75**, wherein the dye is selected from the group consisting of acridine, analine, anthraquinone, arylmethane, azo, diazonium, graphite, indulin, imine, nitro, phthalocyanine, quinone, tetrazolium, thiazole, and xanthene.

78. The marked substrate of claim **75**, wherein the polymer selected from the group consisting of polyvinyl, glucan, glycan, polyester, polysaccharide, polycycloalkylene, polyether, and polyanhydride.

79. The marked substrate of claim **75**, further comprising a self-assembled monolayer formed at an interface on the substrate surface.

80. The marked substrate of claim **79**, wherein the self-assembled monolayer comprises an alkane thiol or a hydroxy-terminal alkane thiol.

81. The marked substrate of claim **79**, further comprising a patterned interface on the substrate surface wherein the self-assembled monolayer is excluded from at least a portion of the patterned interface.

82. A method of applying alignment marks onto reagent array chips, the method comprising:

spotting an array of one or more reagents onto a surface of the chip;

applying an alignment mark composition onto the surface, wherein the reagents are in a fixed register with the alignment mark position; and,

drying the reagents and alignment mark composition;

wherein the mark composition forms one or more water insoluble substantially opaque alignment marks when dried on the chip.

83. The method of claim **82**, wherein the reagent comprises protein, a nucleic acid, a cytokine, a receptor, a pharmaceutical, a virus, a buffer, a co-factor, a modulator, an inhibitor, an activator, a chemical, or a compound.

84. The method of claim **82**, wherein the alignment mark composition is applied concurrent with spotting the reagents.

85. The method of claim **82**, wherein the alignment mark composition comprises a non aqueous solvent.

86. The method of claim **82**, wherein the alignment mark composition comprises a dye.

87. The method of claim **86**, wherein the dye is selected from the group consisting of acridine, analine, anthraquinone, arylmethane, azo, diazonium, graphite, indulin, imine, nitro, phthalocyanine, quinone, tetrazolium, thiazole, and xanthene.

88. The method of claim **87**, wherein the dye is present in an amount ranging from about 1 weight percent to about 20 weight percent of the total composition.

89. The method of claim **88**, wherein the dye is present in an amount ranging from about 3 weight percent to about 15 weight percent of the total composition.

90. The method of claim **89**, wherein the dye is present at about 10 weight percent of the total composition.

91. The method of claim **82**, wherein the alignment mark composition comprises a polymer excipient.

92. The method of claim **91**, wherein the polymer selected from the group consisting of polyvinyl, glucan, glycan, polyester, polysaccharide, polycycloalkylene, polyether, and polyanhydride.

93. The method of claim **92**, wherein the polymer is present in an amount ranging from about 0.5 weight percent to about 10 weight percent of the total composition.

94. The method of claim **93**, wherein the polymer is present in an amount ranging from about 1 weight percent to about 5 weight percent of the total composition.

95. The method of claim **94**, wherein the polymer is present at about 2 weight percent of the total composition.

96. The method of claim **82**, further comprising:

aligning a collector with reference to one or more alignment marks;

dissolving one or more dried reagents with a solvent; and,

collecting the dissolved reagents from the chip with the collector;

thereby recovering one or more reagents from the chip.

97. The method of claim **96**, wherein the steps of spotting, applying, drying, aligning, dissolving, collecting, or transferring are carried out using an automated instrument.

98. The method of claim **96**, wherein the solvent comprises DMSO, DMF, alcohols, or acetonitrile.

99. The method of claim **96**, wherein the surface comprises a self-assembled monolayer formed at one or more interfaces.

100. The method of claim **99**, wherein the self-assembled monolayer comprises an alkane thiol or a hydroxy-terminal alkane thiol.

101. The method of claim **99**, further comprising a patterned region on the chip surface wherein the self-assembled monolayer is formed and an unpatterned region wherein the self-assembled monolayer is excluded from at least a portion of the unpatterned region.

102. The array chip of claim **101**, further comprising a second self-assembled monolayer formed in the unpatterned region and substantially excluded from the patterned region.